MOUSE HEPATITIS VIRUS (MHV)

Glen Otto, D.V.M., Associate Professor, Attending Veterinarian

MHV is one of the most common contaminants of research mouse colonies worldwide and has been responsible for the majority of the rare contamination events affecting the clean Stanford mouse colonies during the last eight years. Although constant diligence is needed to keep this pathogen out of mouse colonies, it is a very worthwhile effort. The paragraphs below provide some information about the virus, and most importantly, explain the serious consequences of this viral infection on ongoing biomedical research using mouse models. These adverse effects are the reason that it is so important to follow the established policies regarding quarantine, animal transfers, proper use of micro-isolator caging, attention to sterile changing and handling procedures in hoods, etc.

Mouse hepatitis virus (MHV) is probably the most important pathogen of laboratory mice. Rats may also become infected but only as sucklings and only under experimental conditions. MHV is a single-stranded RNA virus of the family Coronaviridae. It is extremely contagious and is transmitted primarily via aerosol, direct contact, fomites, and, experimentally, via transplantable tumors.

Approximately 25 strains or isolates of MHV have been described and have been classified as either respiratory or enterotropic. Respiratory strains establish in the nasal mucosa, descend to the lungs, and disseminate via the blood throughout the body or ascend along neurons into the nervous system. The intestinal tract is not usually involved.

Enterotropic strains may also become established in the nasal mucosa but often are confined to the intestinal tract and disseminate only locally to the liver, abdominal lymph nodes, and, in rare cases, to the nervous system. Pulmonary involvement is uncommon. Enterotropic strains appear to be the most common form circulating in contemporary mouse populations.

Lesions of MHV are present for 7 to 10 days following infection of immunocompetent mice and are characterized by multifocal necrosis with formation of occasional multinucleate syncytial giant cell. Lesions due to respiratory strains may be observed in the olfactory mucosa, brain, lungs, and liver, while lesions due to enterotropic strains are generally, though not always, confined to the intestinal tract. Lesions caused by either strain tend to be more severe and widespread in immunocompromised mice. Immunocompromised mice also shed the virus for prolonged periods.

Numerous reports document effects of natural or experimental infection with MHV on host physiology and research. In immunocompromised mice, these effects include necrotic changes in several organs, including the liver, lungs, spleen, intestine, brain, lymph nodes, and bone marrow; differentiation of cells bearing T-lymphocyte markers; altered enzyme activities, bilirubin concentration, and antibody responses to sheep erythrocytes in serum; enhanced

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phagocytic activity of macrophages; rejection of xenograft tumors; impaired liver regeneration; and hepatosplenic myelopoiesis.

In immunocompetent mice, reported effects of MHV infection include transient immunostimulation followed by immunodepression; thymic involution; depletion of macrophage subpopulations; alterations in the expression of a variety of host genes; microcytic anemia and changes in ferrokinetics; decreases in lymphocyte proliferative responses, antibody secretion, phagocytic activity, liver regeneration, blood cell production, number of hepatic sinusoidal endothelial cell fenestrae, incidence of diabetes mellitus in nonobese diabetic mice; apoptotic changes in the thymus; increased tumoricidal activity of peritoneal macrophages, hepatic uptake of injected iron, susceptibility or resistance to copathogens, and IFN and IL-12 production; altered hepatic enzyme activity, behavior of ascites myelomas, and expression of cell surface markers on splenic T lymphocytes; molecular mimicry of the host Fc gamma receptor; nerve demyelination; impaired bone marrow pre-B and B cells; induced production of alpha-fetoprotein and antiretinal autoantibodies in serum; and induced macrophage procoagulant activity.

Clearly, natural MHV infection of laboratory mice could affect many scientific studies and seriously compromise the value of these animals as research subjects. Material adapted from Baker, D.G. Clin Microbiol Rev 1998 Apr; 11(2):231-66. Natural pathogens of laboratory mice, rats, and rabbits and their effects on research.

NEW DEPARTMENTAL OFFICE

The Comparative Medicine departmental office has moved! Our new location is room R321 on the third floor of Edwards. Please note that our mail code has changed:

Department of Comparative Medicine
300 Pasteur Drive, Room R321
Mail Code: 5336

All email addresses and phone numbers remain the same.

WORLD WEEK FOR ANIMALS IN LABORATORIES
Linda Cork, D.V.M., Ph.D., Professor and Chair

This is to remind you that “World Week for Animals in Laboratories” is scheduled for the week of April 20 – 28, 2002. Animal activist groups in the U.S. and abroad hold this annual event, and demonstrations and vandalism may accompany it. Please note that it will span two weekends.

We are not aware of planned demonstrations by animal activist groups at Stanford, however, animal activism and vandalism have always been an issue in the San Francisco Bay area and at academic institutions in general. If more details become available, we will contact you.

Please be vigilant. Be especially attentive to unusual events: unusual or threatening telephone calls, unexpected/odd packages, unexplained visitors, and other aspects of security. Please review the enclosed Emergency Notification chart and post it.

If you use or maintain laboratory animals outside of RAF, please review your security procedures. If consultation on security procedures is needed, please call Mr. Reese Zasio, Veterinary Service Center Operations Manager, at 725-3882. For laboratories based at the VA Palo Alto Health Care System, please consult, if needed, with your security department at 493-5000, (1) 65891.

DIAGNOSTIC LAB NEWS
Roberta Moorhead, Lab Manager, Diagnostic Laboratory

Rodent Chemistries

One of the most frequently asked questions in the lab is how much serum sample does it take to run a chemistry panel. The following is a list of the exact amounts that our analyzer pipettes. These amounts do not include sample amounts needed to perform rechecks due to high or low values, mechanical errors or automatic dilutions when values are not in the linear range.

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Although mites have been present in many rooms in the RAF facility since the building was initially populated, they are becoming more of a problem as each year goes by. As the facility has become more crowded, and the amount of in-house breeding increased, the overall prevalence of the parasite has increased proportionally. The Veterinary Service Center (VSC) is considering a campus-wide eradication effort, and labs will learn more about this in the future. This introductory article will provide background information that will be useful as options are considered.

Mite infections are also known as Acariasis. Mites are fairly common parasites of mice and rats. Most mites are species-specific (that is they can only live on one type of host). Mites are arachnids which means they are related to scorpions, spiders and other mites.

Mites, which are commonly found on mice, are of the suborder of arachnids known as Prostigmata (this group includes the common parasites). The common mouse mite species are *Myobia musculi* (Fur Mite of Mouse), *Myocoptes musculinus* (Myocoptic Mange Mite), and *Radfordia affinis* (Fur Mite of Mouse). These mites are fur mites, which means they eat skin debris and skin secretions (oils etc). There is a much rarer mite on mice called *Psorergates simplex* which actual live in the hair follicle.

The most common mite of rats is also from the suborder Prostigmata. The most common species is *Radfordia ensifera* (Fur Mite of Rat). These eat skin debris and secretions of the skin. There is also a very rare species *Notoedres muris* (Ear Mange of Rat Mite).

**Life Cycle:** The life cycle of *Myobia musculi* is the most well known, and it is thought that the others are similar to this, although this is not certain. Eggs hatch in 8 days. Larvae hatch from these eggs and moulting developing into the adult stage. The life cycle is believed to be at least 13 days. The duration of this life cycle explains why multiple treatments are needed. Adult Tropical Rat Mites can live up to 70 days.

**Transmission:** Transmission of all these mites is through direct contact with infected animals, bedding, cages and food. It is therefore important to quarantine new animals and treat any suspect ones. Keep your pets away from contact with wild rats and mice. As bedding is infected it should be treated at the same time as the animals.
Laboratory animals are expected to attend this training. These half-day seminars are held in Munzer Auditorium, from 12:30 – 4:00 p.m. The next two seminars have been scheduled for:

Wednesday, April 24, 2002
Wednesday, June 12, 2002

To register online, visit the Department of Comparative Medicine’s web site:
www.med.stanford.edu/school/CompMed
Select Veterinary Service Center (VSC), then Training/Education Events found under General Information. Just choose the date you wish to attend and complete the registration form. You can always find upcoming training events on this web site as well as a description of the different types of training available.

If you have any questions regarding the Department of Comparative Medicine’s training programs, please contact Jennifer Lee at 725-9901 or jlee3@stanford.edu.

NEW DIRECTOR OF FINANCE AND ADMINISTRATION

The Department of Comparative Medicine is pleased to welcome its new departmental Director of Finance and Administration, Peter S. Jakovich. Peter has an extensive background in business and academia. He received his M.B.A. from Pepperdine University and worked in industry for almost ten years. He left the corporate life to become Dean of Business Affairs at El Camino College, a large junior college in Torrance, during the late 70s. After returning to industry for another ten years, he opened his own thriving management consulting business in the 80s. We are delighted that he has decided to return to academia.

Peter can be found in R318 in our new administrative offices on the 3rd floor of the Edwards Building. His phone number is 725-3874 and his email address is jakovich@stanford.edu.

UPCOMING TRAINING DATES
Jennifer Lee, Training Coordinator

The Animal Care and Use training seminar is an introduction to the care and use of laboratory animals in research and teaching at Stanford University. All faculty, staff and students who will be involved in the use of laboratory animals are expected to attend this training. These half-day seminars are held in Munzer Auditorium, from 12:30 – 4:00 p.m. The next two seminars have been scheduled for:

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TO EVERYONE WHO WORKS IN A LABORATORY ANIMAL FACILITY

Jim Boardman, The Jackson Laboratory

My name is Jim Boardman and I work for The Jackson Laboratory. Like many people in the laboratory animal science profession, I am sometimes cautious when someone asks me what I do for a living. I am proud of what I do, but if the person is someone I need to deal with in some other aspect of my life, I would prefer that what I do for a living not be a potential source of conflict. Last spring, I received a lesson in confidence building that will stay with me for a long time.

I was returning home from a business trip and the time of my arrival and the route home corresponded nicely with the need to pick up my youngest son from his gymnastics lesson. As I waited, another father, also wearing a suit and having shed his ties, commented that it was always interesting to return from a trip to find that the weather had changed from sunshine to snow in such a short time.

I agreed, and we exchanged introductions and pleasantries. When he asked me what I did for a living I hesitated, but only for a minute, and then told him that I worked for an organization that conducted genetic research and distributed mice for medical and scientific study.

There, now he knew. His expression never changed, and he asked rather matter-of-factly if we had any mice for studying cystic fibrosis. Before I could answer him, several dozen boisterous 9-year-olds burst from within the gym and we both became caught up with trying to find a matching pair of socks and a water bottle to take home. Later, outside on the walk, I saw the other dad again and told him that I would get some information for him.

When I got home I mentioned the conversation to my wife, but I couldn’t remember the name of the man I had been speaking with or the name of his son. It didn’t matter, because my wife knew immediately whom I had been talking to. During her many, many, many trips to the gym, she had spoken several times to the man’s wife. They had a 12-year-old daughter named Maggie who had cystic fibrosis and spent about one week of every month in the hospital having her lungs cleaned. Their family’s routine included the usual car pools and school events, but also a lot of home care and many visits to the hospital and doctor’s office.

I went to the JAX web site and located several models available for cystic fibrosis research. After reviewing the information, I began to have second thoughts about passing it along to the father because the prognosis for the animals was quite grim. My wife told me that she was confident that they were well aware of the complications and progression of the disease and that they would welcome any information they could get. So I printed it.

The following weekend our home gym hosted a gymnastics meet. Amid the excitement of the first day of the event I managed to discreetly hand the envelope to the father and told him that I hoped he would find the content informative. The rest of the day went by quickly. The boys competed, got their medals and we all went home.

The next day my youngest son was competing. When I arrived I saw the father again. He came over to me and told me that he had spoken to Maggie about the information I had given him. And she was excited. She was happy to know that there was a mouse that could be used to study her disease and that her dad actually knew someone who sold it. I don’t get warm, fuzzy feelings very often, but I got one then. The look on his face and the unspoken gratitude in his voice really made my day.

As you spend your days in your animal room, or the office, or the cage wash, feeling weary and unappreciated, please remember one thing. The people who are the ultimate beneficiaries of your work are not in a position to say “thank you.” But your work doesn’t just make their day. It means the whole world to them. Keep up the good work. Reprinted by permission from the American Association for Laboratory Animal Science.